Amendments to the Specification:

Please replace the final paragraph of page 29 with the following paragraph:

As shown in Fig. 1, PDK1 is mainly localized in CYT following our fractionation protocol. ~~Its indisputably soluble nature is supported by the fact that it resists pelleting~~

Please replace the paragraph of page 31 with the following paragraph and renumber as page 30:

~~HiP by immunoblot analysis (Fig. 11) revealed that Ext-HiP was greatly enriched in paxillin, vinculin, actin, and the actin-associated protein Arp3. In contrast, this fraction appeared to contain less integrin □1 receptor than the PM and PM(SW) fractions.~~ Interestingly, ILK, which has also been shown to be present in focal adhesion (Dedhar, 1999), was not enriched in Ext-HiP. A comparison between PM and PM(SW) indicated that 1 M NaCl removed some ILK from the membrane, but we found that like a typical peripheral protein, the ILK extracted with high salt predominantly localized to the Ext-HiS and not to the Ext-HiP (data not shown). Similar to our earlier observations, the distribution of ILK did not correlate with the observed PDK2 activity. The localization of PDK1 was ambiguous since PDK1 in the PM fraction appeared as two bands. The lower band, which co-migrates with cytosolic PDK1, was enriched in Ext-HiP. The upper band, which represents the more abundant PDK1 signal in the PM, was de-enriched in the Ext-HiP. However we do not know whether the upper signal is due to a modified form of PDK1 or just a cross-reacting protein. The insulin receptor remained associated with the PM(SW) and was essentially absent from Ext-HiP. Caveolae are cholesterol-rich invaginations

Amendments to the Specification (continued):

abundant in the plasma membranes of 3T3-L1 adipocytes and are important in the insulin-stimulated cbl-CAP pathway (Watson, 2001). Caveolin, a major protein in caveolae, however, was not enriched in Ext-HiP. We conclude from these results that the PM(SW) most likely contained the majority of the actual membrane comprising of the phospholipid bilayer, integral membrane proteins, and caveolae while Ext-HiP, the fraction that contained the bulk of the PDK2 activity in the PM, was enriched in cytoskeletal elements particularly focal adhesions. Incubation in 1 M NaCl disrupted the association between the cytoskeleton and the plasma membrane thereby allowing them to be segregated by centrifugation. Co-localization of PDK2 in focal adhesions is consistent with the previous observation that the integrin receptor signal transduction pathway activates Akt (Khwaja, 1997).